The Role of Backbone Oxygen Atoms in the Organization of Nucleic Acid Tertiary Structure: Zippers, Networks, Clamps, and C–H···O Hydrogen Bonds

Imre Berger and Martin Egli*

Abstract: Tight packing between structural elements is a prerequisite for molecular recognition and catalysis. In proteins, α-helices and β-sheets present the amino acid side chains on the surface while the polar amide bonds are buried. The opposite is found in double- and polystranded nucleic acids, where negatively charged phosphates occupy the surface and the side chains are hydrogen bonded in the core. Thus the question arises: How do densely packed nucleic acid molecules achieve close approach, despite the repulsion between phosphates that would appear to preclude tight contacts? One obvious answer is by mediating interstrand contacts through coordinated cations that can screen the negative charges. In this contribution, however, we highlight a variety of alternative direct interactions involving atoms of the sugar–phosphate backbone that can promote tight packing of RNA and DNA into functional molecules. We have analyzed the existing nucleic acid crystal structures in terms of the presence of close contacts between backbone regions. In RNA, ribose 2′-hydroxyl groups were observed to mediate such contacts in the majority of cases. However, their absence in DNA does not prevent oligodeoxynucleotides from packing tightly, aided by various interactions between backbone atoms.

Keywords: DNA structures · hydrogen bonds · nucleic acids · RNA · tertiary structure

Introduction

The three-dimensional structure of a large RNA molecule, the P4–P6 domain of *Tetrahymena thermophilia* group I self-splicing intron, features a sharp bend, generating side-by-side packing of helices. The recently determined X-ray crystal structure of this 160-nucleotide fragment has provided a detailed picture of the tertiary interactions stabilizing this fold.[1] Along with several metal–ion binding sites, numerous novel structural motifs were observed.[2, 3] In particular, ribose zippers, formed by adjacent pairs of hydrogen-bonded ribose 2′-hydroxyl groups, were shown to mediate direct contacts between the sugar–phosphate backbones of neighboring helices. When the first structure of a large ribonucleic acid molecule, $tRNA^{Phe}$, was determined at atomic resolution, it became immediately clear that the 2′-hydroxyls play a key role in the stabilization of RNA tertiary structure.[4] The intron domain, being only the third structure of a large RNA molecule (after tRNA and the hammerhead ribozyme) to be determined by X-ray crystallography to date, thus underscores this crucial function of the ribose 2′-hydroxyl group, the chemical moiety that distinguishes RNA from DNA. Through conferring a large number of water molecules on the RNA backbones and grooves, the 2′-hydroxyl groups are furthermore responsible for the higher thermodynamic stability of the RNA duplex compared with DNA.[5] In fact, incorporation of single 2′-hydroxyl groups in otherwise all-deoxy DNA duplexes has been demonstrated to convert the duplex conformation from the regular B- to the A-form typical for RNA.[6, 7] Moreover, specific 2′-hydroxyl groups were shown to be important for protein–RNA[8] and RNA–RNA recognition.[9]

Interestingly, the essential structural features of the ribose zipper motif are also present in the crystal structure of an RNA oligonucleotide duplex.[10, 11] The observation that functional groups of the sugar–phosphate backbone can contribute to the stabilization of a particular fold in a large RNA domain and that similar hydrogen-bonding patterns also exist in the crystal lattices of small RNA fragments prompted us to examine the crystal structures available in the Nucleic Acid Database[12] for further stabilizing direct contacts involving atoms of the sugar–phosphate backbone. Although the crystal structure of the P4–P6 domain constitutes the first example of an RNA large enough to display intramolecular side-by-side helical packing, a similar intermolecular arrangement of helices is not uncommon in crystal structures of RNA oligonucleotide fragments.[13]

In the following paragraphs, we provide examples of direct hydrogen-bonding interactions in crystal structures of RNA oligonucleotides that involve the sugar–phosphate backbone. In most cases, the specific contacts we found involve the RNA 2′-hydroxyl group. We compare them to similar interactions in

[*] M. Egli
Drug Discovery Program and
Dept. of Molecular Pharmacology and Biological Chemistry
Northwestern University Medical School, 303 East Chicago Avenue, Chicago, IL 60611-3008 (USA)
Fax: Int. code +(312)503-0796
e-mail: m-egli@nwu.edu

I. Berger[+]
Dept. of Biology, Massachusetts Institute of Technology
Cambridge, MA 02139 (USA)

[+] New address: Institute for Molecular Biology and Biophysics
ETH-Hönggerberg, 8093 Zürich (Switzerland)

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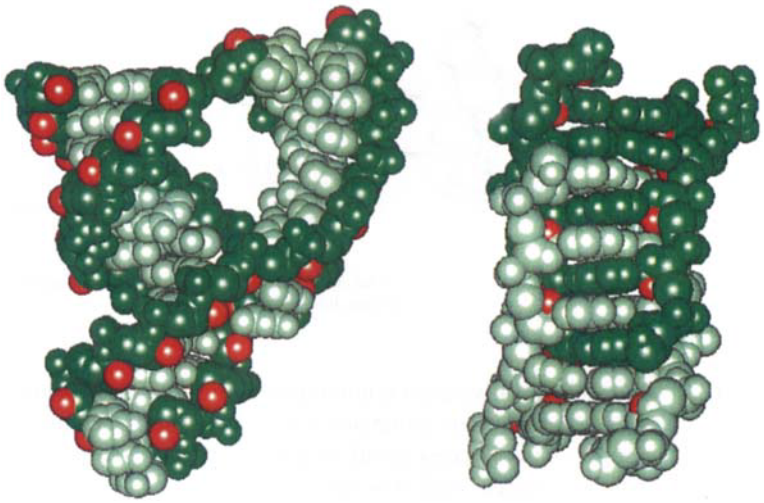

Figure 1. Recently determined nucleic acid structures. Left: hammerhead-ribozyme [18,19] (backbone and base atoms dark green and light green, respectively; 2′-oxygens red). Right: C-rich i-motif ("intercalated") DNA [22–24] (atoms in the two parallel-stranded duplexes dark green and light green, respectively; 4′-oxygens red).

the structures of two larger RNAs, the hammerhead ribozyme (Figure 1, left) and the group I intron P4–P6 domain (Figure 2a). In addition, we illustrate, based on hydrogen-bonding interactions observed in the crystal structures of DNA fragments (e.g. the C-rich self-intercalated quadruplex motif, Figure 1b), that deoxynucleic acid, despite the lack of the versatile ribose 2′-hydroxyl group, can in fact overcome this handicap, and is also able to tolerate close contacts between backbones through a variety of hydrogen-bonding interactions involving the deoxyribose sugar atoms.

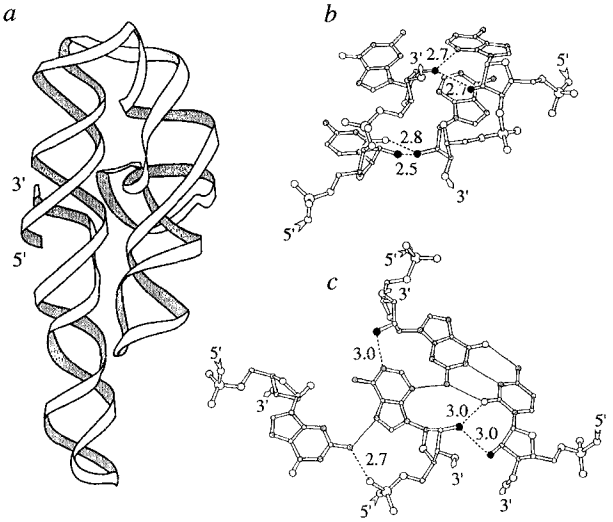

Figure 2. RNA backbone interactions: a) Overall fold of the P4–P6 group I intron domain [1,2]. b) Example of an O2′ ribose zipper (intron domain; 2′-oxygens black, hydrogen bonds dashed). c) Base–O2′ interactions, intron domain.

Discussion

RNA: In the P4–P6 domain structure, numerous close contacts occur between the sugar–phosphate backbones of individual regions. All of them involve segments of the molecule whose conformations deviate from the standard A-type helical structure typical for regular RNA duplex molecules. The sharp turn at the apex of the structure for instance is stabilized by an adenosine-rich bulge that is packed against the minor groove of the neighboring stem (Figure 2a, center). A characteristic feature of this bulge is that the bases are turned inside out with the phosphates coordinated to two magnesium ions in the core.[2] Interestingly, this arrangement is somewhat reminiscent of the structural model for DNA proposed by Pauling and Corey,[14] featuring the bases on the surface and the negatively charged phosphates on the inside, with metal ions compensating for Coulomb repulsion. The specific arrangement of a portion of this bulge in the minor groove of the adjacent stem enables two consecutive riboses from adenosine residues to pair with riboses from cytidine and guanosine residues of the neighboring stem (Figure 2b) through their 2′-hydroxyl groups (O2′ atoms filled in black throughout). The hydrogen-bonding interactions between the ribose pair are asymmetric in the sense that the 2′-oxygen from the cytidine residue (Figure 2b, lower left) interacts only with the 2′-oxygen of the adjacent adenosine (Figure 2b, lower right), which in turn is involved in a bidentate hydrogen bond to the minor groove base function of the adjacent cytidine residue. The same pattern, though reversed, exists between the guanosine and adenosine residues paired in the second step of this ribose zipper. A further asymmetry arises from the fact that the cytidine and guanosine riboses forming one half of the zipper are part of a canonical A-stem, while the adenosine sugars are situated in a single-stranded bulge. A very similar pattern of ribose pairing is found in another region of the P4–P6 domain, with two backbones approaching each other closely (Figure 2a, bottom of the helix on the right). Here, a hairpin tetraloop with the sequence GAAA reaches into the minor groove of the adjacent duplex region, the tetraloop receptor.[1] The resulting ribose zipper involves ribose sugars from adenosine residues in the tetraloop on the one hand and ribose sugars from uridine and guanosine residues from the receptor on the other.

Pairwise hydrogen bonding between 2′-hydroxyl groups was also observed in the crystal structure of the RNA duplex formed by the sequence $U(UA)_6A$.[15] In this crystal lattice, the minor groove of one duplex is spanned by the backbone of a neighboring, symmetry-related molecule (Figure 3a). However, in con-

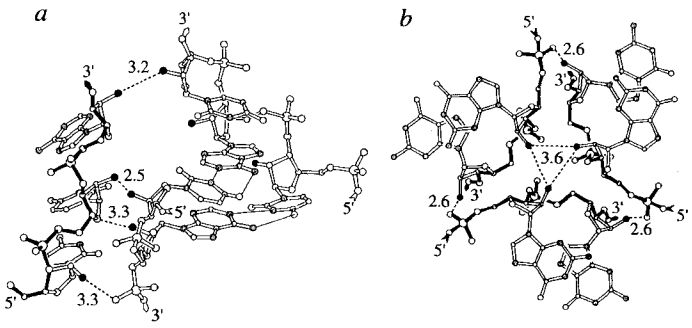

Figure 3. RNA backbone interactions: a) Two-helix junction, $U(UA)_6A$ [11,15]. b) Three-helix junction, C_4G_4 [16].

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trast to the situation in the P4–P6 group I intron domain, this interaction takes place between canonical A-form double helices and thus gives rise to a two-helix junction. The pairing does not involve any contacts between 2′-hydroxyls and bases, as the sugar–phosphate backbone segment crossing the minor groove of the adjacent duplex does not penetrate this groove sufficiently. Another close backbone–backbone contact mediated by 2′-hydroxyls is present in the crystal structure of the RNA octamer $r(C_4G_4)$.[16] This junction actually involves three tightly packed duplexes. The close arrangement of strands around a crystallographic threefold axis is stabilized by direct hydrogen bonding between 2′-hydroxyls and additional interactions between 2′-hydroxyls and phosphate groups at adjacent sites (Figure 3b). These examples clearly underscore the important role of the 2′-hydroxyl groups in mediating close backbone–backbone interactions, and illustrate the numerous ways how the ribose zipper and related motifs can provide for the tight intra- and intermolecular packing of RNA molecules.

Being the only functional group in the sugar–phosphate backbone capable of acting as both an acceptor and a donor for hydrogen bonds, the RNA 2′-hydroxyl group can interact with backbone and base sites in many other ways besides the ribose zipper motif. For example, a three-way junction formed in the region of the adenosine-rich bulge in the P4–P6 domain (Figure 2a, center) features an adenosine residue nested against the minor groove of the adjacent helix region, forming a base triple with a Watson–Crick C·G base pair. 2′-Hydroxyl groups participate extensively in the network of hydrogen bonds that stabilize this junction, which involves a second guanosine residue (Figure 2c). The 2′-hydroxyl groups mediate intricate interresidue contacts through forming numerous hydrogen bonds to bases, phosphate oxygens, and other 2′-hydroxyl groups, thus leading to a dramatic extension of the usually encountered pairing schemes between bases. The list of backbone interactions involving 2′-hydroxyl groups could easily be extended. In particular, the sharp turn characterizing the structure of the P4–P6 domain (Figure 2a) is stabilized by several O2′-phosphate and O2′-base hydrogen-bonding interactions as well.

Two further rather frequently encountered folding motifs in RNA molecules are the so-called U-turn, first observed in $tRNA^{Phe}$, and the GNRA tetraloop (R: purine, N: any base). Structural features common to both have recently been pointed out and have inspired the notion that GNRA tetraloops will in fact form a sharp bend resembling a U-turn.[17] In the $tRNA^{Phe}$ crystal structure, the U-turn occurs in the anticodon loop and the T-loop. It came as a major surprise that the hammerhead ribozyme also features the U-turn motif at a functionally important location, namely, adjacent to the cleavage site.[18, 19] Conformational characteristics as well as conserved interactions in the U-turn motif are illustrated in Figure 4a (see also ref. [17]), depicting the GUAA tetraloop[19] in the hammerhead ribozyme (Figure 1a, bottom). The sharp turn in the backbone goes along with the formation of a hydrogen bond between the imino proton of the guanine (*G*NRA) and a phosphate oxygen atom (GNR*A*). In addition, a hydrogen bond is formed between the 2′-hydroxyl of the guanosine ribose and the N7 of an adenosine (GN*R*A). Perhaps the most striking feature of the U-turn motif is the phosphate group (GN*R*A) sitting on top of the guanine base. As pointed out in some detail below, this stabilizing

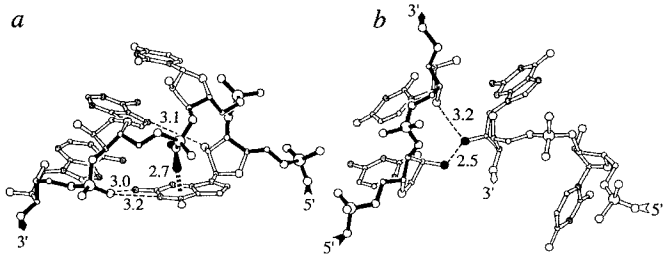

Figure 4. RNA backbone interactions: a) U-turn, hammerhead (oxygen lone pairs black) [19]. b) O4′···O2′ interactions, hammerhead.

$n \rightarrow \pi^*$ conjugative effect is not only restricted to the interaction between a phosphate group and a base, but is also operative in a sugar–base stacking motif frequently encountered in noncanonical nucleic acid structures.[20, 21] The geometry of the U-turn motif is particularly enlightening in terms of how RNA overcomes repulsion between negatively charged phosphates that could result from tight turns in the backbone, or close backbone–backbone interactions in general. In addition to the interactions within the U-turn motif, the wishbone-like overall structure of the hammerhead ribozyme (Figure 1a) is stabilized by many contacts between 2′-hydroxyls and base atoms in the core. An interesting set of interactions is depicted in Figure 4b, featuring a guanosine residue forming hydrogen bonds via its 2′-OH to both the 2′-hydroxyl and a ribose 4′-oxygen from consecutive residues of an adjacent strand; this highlights the potential of the 4′-oxygen atom to participate in mediating close backbone contacts as well.

DNA: DNA, in contrast to RNA, lacks the hydroxyl group at the 2′-position of its deoxyribose sugar ring. Thus, it was reasoned that DNA by its chemical nature would be less apt to form tertiary interactions mediated by the sugar phosphate backbone.[1] However, careful investigation of nucleic acid crystal structures reveals that DNA can bypass the lack of a 2′-hydroxyl group in an elegant fashion. By utilizing the 4′-Oxygen atom of the deoxyribose sugar ring, in addition to oxygen atoms of the phosphodiester linkage, DNA is indeed able to allow for close-packing contacts between nucleic acid molecules.

Systematic interactions involving 4′-oxygen atoms were observed in crystals of four-stranded intercalated cytosine-rich DNA, an unusual nucleic acid motif recently described.[22–24] In these structures with stretches of cytidine residues, two parallel DNA duplexes, each forming hemiprotonated cytosine·cytosine$^+$ ($C\cdot C^+$) base pairs, are intercalated into each other with opposite polarity to form a quadruplex. Conserved features of this quadruplex structure are a slow, right-handed helical twist of 12–20°, an average stacking distance of 3.1 Å and the existence of two broad and two narrow grooves.[23, 24] A characteristic cross-section through the four-stranded intercalated C-rich motif including two adjacent $C\cdot C^+$ base pairs is displayed in Figure 5a. This representation illustrates the lack of stacking between the cytosine heterocycles of neighboring base pairs. Stacking is confined to the exocyclic keto and amino groups of the cytosines, resulting in a stacking distance between adjacent $C\cdot C^+$ base pairs of approximately 3.1 Å. This is less than the 3.4 Å stacking distance encountered in regular B-DNA, where overt stacking of the aromatic rings occurs. A striking

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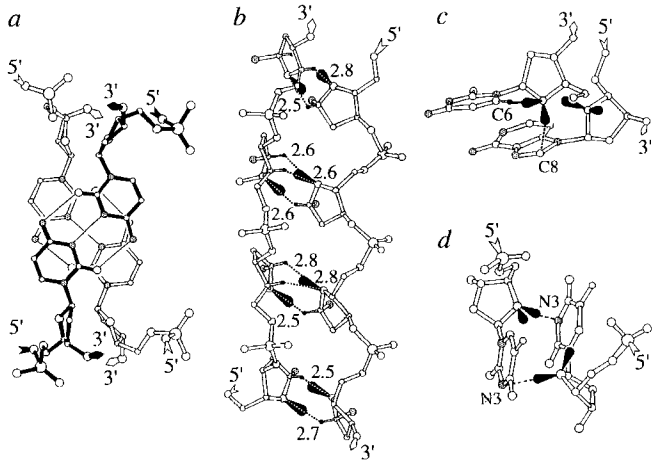

Figure 5. DNA backbone interactions: a) Cross-section of the i-motif quadruplex [20]. b) C–H···O zipper in the narrow groove of the i-motif (C1′ and C4′ hydrogens and 4′-oxygen lone pairs black, hydrogen bonds dashed). c) Sugar-base stacking I, i-motif. d) Sugar–base stacking II, i-motif.

feature is the close proximity of the deoxyribose sugar rings in the narrow grooves on both sides of the molecule. In fact, adjacent O4′ atoms in these narrow grooves are positioned at hydrogen bonding distance to the H1′ (and in some cases also H4′) hydrogen atoms of the neighboring sugar ring. Thus, a systematic network of hydrogen bonds involving H1′, O4′, and in some cases H4′ atoms is found in the narrow grooves of the molecule (Figure 5b). This C–H···O hydrogen-bond zipper links closely spaced backbones of the intercalated parallel duplexes and illustrates an elegant possibility to bring DNA strands in close proximity through their sugar–phosphate backbones. Another example of closely spaced DNA backbones involving C–H···O hydrogen bonding was observed in the recently reported crystal structure between the anticancer drug cisplatin and a DNA duplex.[25] In that structure, a series of hydrogen bonds were found between C4′–H and a nonbridging phosphate oxygen on the one hand and between O3′ and C5′-H on the other.

Crystals of four-stranded intercalated DNA revealed two further examples of O4′-mediated close contacts (Figures 5c and 5d). One of these, the stacking of a sugar on a base, can be interpreted as an $n \rightarrow \pi^*$ conjugative effect, as illustrated in Figure 5c for a deoxyribose O4′ lone pair and the C8=N7 double bond from a stacked adenine base.[20, 21] This Figure also depicts an intracytidine O4′···H6–C6 hydrogen bond. Similar $n \rightarrow \pi^*$ interactions occur between closely spaced thymidine residues. Here, the 4′-oxygen lone pair of one thymidine residue is positioned approximately normal to the base plane of the neighboring residue and vice versa (Figure 5d). This is consistent with the existence of partial N3=C2 and N3=C4 double bonds and the positioning of the O4′ lone pairs between the π^* orbitals associated with them.[20] Interactions of this kind are regularly observed in crystals of A-DNA fragments, where the base-on-ribose stacking between terminal base pairs of the A-form duplexes that rest in the shallow minor grooves of adjacent molecules actually appears to be the main intermolecular interaction stabilizing the three-dimensional crystal lattice.

In crystals of DNA fragments that form short B-type helices, an interaction of a different kind is observed, involving phosphate oxygen atoms of the phosphodiester linkage of the backbone.[26, 27] In these crystal structures, stacked B-DNA duplexes form infinite quasi-continuous helices. Unlike in the case of the majority of DNA oligonucleotide crystals, the infinite helices here are not aligned in a coaxial fashion in the lattice, but cross at an angle next to each other forming regions of close contact between adjacent DNA duplex molecules. The "intersection" formed by two infinite helices in the crystal is shown in Figure 6a in a ribbon representation. This arrangement is reminiscent of the situation associated with genetic recombination, where a crossover between adjacent DNA duplexes occurs at so-called Holliday junctions.[26, 27] The detailed contacts formed between two adjacent duplexes at the intersection are shown in Figure 6b. Two backbone phosphate oxygen atoms from a duplex in one infinite helix (only a section is shown with black bonds) form hydrogen bonds to the N4 amino groups of cytosine bases in the major groove of a neighboring DNA duplex (two adjacent base pairs are depicted). Thus, the cytidine residues build a tight "clamp" around the phosphate oxygen atoms of a neighboring sugar phosphate backbone, forming a specific major groove–backbone interaction between adjacent DNA molecules. Similar interactions were observed in other crystal structures of B-DNA fragments and a possible role in DNA self-recognition has been implied for such molecular clamps.[28, 29]

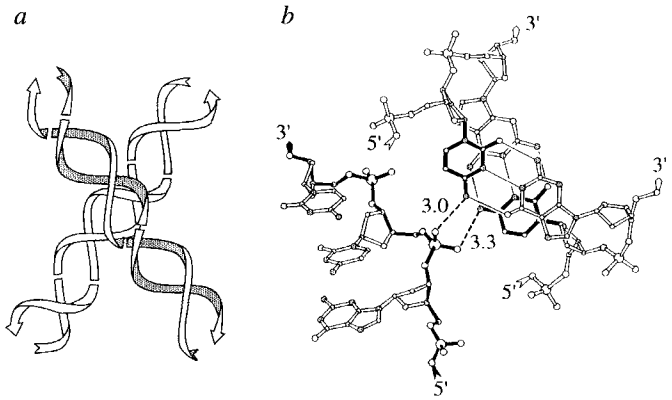

Figure 6. DNA backbone interactions: a) Diagonally packed B-DNA helices, d(CCGGCGCCGG) [26]. b) Molecular clamp at the intersection of duplexes.

In crystals of coaxially packed helical DNA fragments, water molecules or hydrated metal ions were often observed to mediate indirect contacts between closely spaced molecules by bridging backbone oxygen atoms of the phosphodiester linkage. In contrast, in crystals of side-by-side arranged left-handed Z-type duplexes (Figure 7a), phosphate oxygen atoms were found to form direct close contacts with duplexes of neighboring infinite helices. A detail of the interaction involving a phosphate group and a guanine base from closely spaced Z-DNA duplexes is shown in Figure 7b. Guanines in Z-DNA with alternating dG–dC sequence appear to be electronically strongly polarized. This is consistent with the Z-DNA-specific coordination of metal or organic cations to O6 and N7 atoms of the guanine base, and also with the observation of extensive intramolecular base-on-ribose stacking involving the guanine heterocycle in Z-DNA crystal structures.[21] The polarization of the guanine

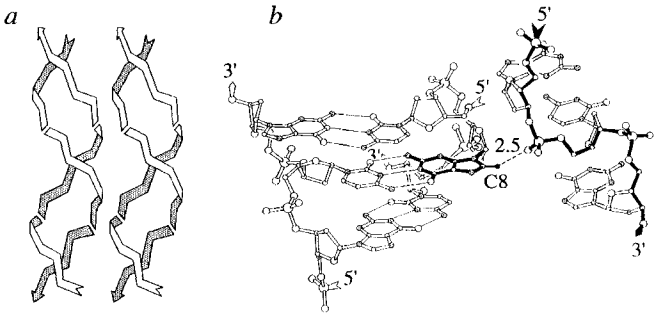

Figure 7. DNA backbone interactions: a) Side-by-side packed Z-DNA helices, $d(CG)_3$ [21]. b) C–H···O hydrogen bond at the interface between duplexes.

base in Z-DNA is thought to give rise to a partially positively charged C8 carbon, rendering its hydrogen slightly acidic. Evidence for this is provided by adjacent negatively charged phosphate oxygen atoms that are located at distances from the C8 carbon that are consistent with the formation of a C–H···O hydrogen bond to the H8 hydrogen atom as depicted in Figure 7b. This interaction occurs systematically in crystals of left-handed Z-DNA fragments, and provides another example of close contacts between tightly packed nucleic acid molecules mediated by backbone atoms other than the RNA 2′-hydroxyl group.

Conclusion

The interactions described in this contribution, involving various backbone oxygen and hydrogen atoms, highlight recurrent stable motifs in nucleic acid structures. They are likely to be encountered frequently in large and elaborately folded molecules, both RNA and DNA. Each interaction represents a way to stabilize close contacts between backbones, or backbones and bases, that allow for tight packing of adjacent nucleic acid molecules or their structural domains. It is of particular interest that the chemically uniform, repetitive sugar–phosphate backbone may contribute in various ways to a selective and potentially even specific self-recognition of neighboring nucleic acid segments, making versatile use of O2′, O4′ and phosphate oxygen atoms.

Nucleic acids are currently the focus of intensive research efforts, as potent catalysts of many chemical reactions as well as specific diagnostic markers for numerous biologically relevant molecules, including those on the surface of cancerous cells. Detailed knowledge of the nature of the inter- and intramolecular interactions governing the structural assembly of nucleic acids besides the known base-pairing rules will be invaluable, not only for more accurate folding predictions of important RNA and DNA molecules in the cell, but also for a rational de novo design of aptamers and catalytic nucleic acid molecules, tailor-made to recognize a particular epitope or catalyze a specific chemical reaction.

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[1] J. H. Cate, A. R. Gooding, E. Podell, K. Zhou, B. L. Golden, C. E. Kundrot, T. R. Cech, J. A. Doudna, *Science* **1996**, *273*, 1678–1685.
[2] J. H. Cate, A. R. Gooding, E. Podell, K. Zhou, B. L. Golden, A. A. Szewczak, C. E. Kundrot, T. R. Cech, J. A. Doudna, *Science* **1996**, *273*, 1696–1699.
[3] a) J. H. Cate, J. A. Doudna, *Structure* **1996**, *4*, 1221–1229; b) J. H. Cate, H. L. Raven, J. A. Doudna, *Nat. Struct. Biol.* **1997**, *4*, 553–558.
[4] G. J. Quigley, A. Rich, *Science* **1976**, *194*, 796–806.
[5] M. Egli, S. Portmann, N. Usman, *Biochemistry* **1996**, *35*, 8489–8494.
[6] M. Egli, N. Usman, A. Rich, *Biochemistry* **1993**, *32*, 3221–3237.
[7] C. Ban, B. Ramakrishnan, M. Sundaralingam, *J. Mol. Biol.* **1994**, *236*, 275–285.
[8] K. Musier-Forsyth, P. Schimmel, *Nature* **1992**, *357*, 513–515.
[9] U. von Ahsen, R. Green, R. Schroeder, H. F. Noller, *RNA* **1997**, *3*, 49–56.
[10] F. Michel, E. Westhof, *Science* **1996**, *273*, 1676–1677.
[11] A. C. Dock-Bregeon, B. Chevrier, A. Podjarny, D. Moras, J. S. deBear, G. R. Gough, P. T. Gilham, J. E. Johnson, *Nature* **1988**, *335*, 375–378.
[12] H. M. Berman, W. K. Olson, D. L. Beveridge, J. Westbrook, A. Gelbin, T. Demeny, S.-H. Hsieh, A. R. Srinivasan, B. Schneider, *Biophys. J.* **1992**, *63*, 751–759.
[13] M. Egli, S. Portmann, D. Tracz, C. Workman, N. Usman, *Acta Crystallogr. D* **1995**, *51*, 1065–1070.
[14] a) L. Pauling, R. B. Corey, *Nature* **1953**, *171*, 346; b) L. Pauling, R. B. Corey, *Proc. Natl. Acad. Sci. U. S. A.* **1953**, *39*, 84.
[15] A. C. Dock-Bregeon, B. Chevrier, A. Podjarny, J. E. Johnson, J. S. deBear, G. R. Gough, P. T. Gilham, D. Moras, *J. Mol. Biol.* **1989**, *209*, 459–474.
[16] S. Portmann, N. Usman, M. Egli, *Biochemistry* **1995**, *34*, 7569–7575.
[17] F. M. Jucker, A. Pardi, *RNA* **1995**, *1*, 219–222.
[18] H. W. Pley, K. M. Flaherty, D. B. McKay, *Nature* **1994**, *372*, 68–74.
[19] W. G. Scott, J. T. Finch, A. Klug, *Cell* **1995**, *81*, 991–1002.
[20] I. Berger, M. Egli, A. Rich, *Proc. Natl. Acad. Sci. U. S. A.* **1996**, *93*, 12116–12121.
[21] M. Egli, R. V. Gessner, *Proc. Natl. Acad. Sci. U. S. A.* **1995**, *92*, 180–184.
[22] K. Gehring, J.-L. Leroy, M. Guéron, *Nature* **1993**, 363, 561–565.
[23] I. Berger, C. H. Kang, A. Fredian, R. Ratliff, R. Moyzis, A. Rich, *Nature Struct. Biol.* **1995**, *2*, 416–425.
[24] C. H. Kang, I. Berger, C. Lockshin, R. Ratliff, R. Moyzis, A. Rich, *Proc. Natl. Acad. Sci. U. S. A.* **1994**, *91*, 11636–11640.
[25] P. M. Takahara, C. A. Frederick, S. J. Lippard, *J. Am. Chem. Soc.* **1996**, *118*, 12309–12321.
[26] U. Heinemann, C. Alings, M. Bansal, *EMBO J.* **1995**, *11*, 1931–1939.
[27] D. S. Goodsell, K. Grzeskowiak, R. E. Dickerson, *Biochemistry* **1995**, *34*, 1022–1029.
[28] Y. Timsit, E. Westhof, R. P. P. Fuchs, D. Moras, *Nature* **1989**, *341*, 459–462.
[29] Y. Timsit, D. Moras in *Biological Structure and Dynamics Vol. 2* (Eds.: R. H. Sarma, M. H. Sarma), Adenine Press, New York, **1996**, pp. 235–246.

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